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2 **CLAIMS**
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4 1. A method of treating rhinosinusitis or alleviating the symptoms of rhinosinusitis,
5 comprising

6 administering an agent that permits the release of proteins from the endoplasmic
7 reticulum.
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9 2. The method of claim 1, wherein the agent is delivered intranasally.
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11 3. The method of claim 1, further comprising the step of:
12 providing an individual suffering from rhinosinusitis.
13

14 4. The method of claim 3, wherein the providing step comprises providing an individual
15 suffering from chronic rhinosinusitis.
16

17 5. The method of claim 3, wherein the individual carries a mutation in at least one copy of a
18 gene encoding a cystic fibrosis transmembrane conductance regulator.
19

20 6. The method of claim 3, wherein the gene is the *CFTR* gene.
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22 7. The method of claim 3, wherein the individual carries a mutation in one copy of the gene.
23

24 8. The method of claim 3, wherein the individual carries a mutation in both copies of the
25 gene.
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27 9. The method of claim 7 or claim 8, wherein the mutation is a $\Delta F508$ mutation.
28

29 10. The method of claim 9, wherein the individual carries an M470V variant of the *CFTR*
30 gene.
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1 11. A method of treating hemochromatosis or alleviating the symptoms of hemochromatosis,
2 comprising
3 administering an agent that permits the release of proteins from the endoplasmic
4 reticulum.

5
6 12. The method of claim 11, further comprising the step of:
7 providing an individual suffering from hemochromatosis.

8
9 13. The method of claim 11, wherein the providing step comprises providing an individual
10 having a mutation in at least one copy of a gene encoding an HFE protein.

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12 14. The method of claim 12, wherein the individual carries a mutation in one copy of the
13 gene.

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15 15. The method of claim 12, wherein the individual carries a mutation in both copies of the
16 gene.

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18 16. A method of treating Gitelman's syndrome or alleviating the symptoms of Gitelman's
19 syndrome, comprising
20 administering an agent that permits the release of proteins from the endoplasmic
21 reticulum.

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23 17. The method of claim 16, further comprising the step of:
24 providing an individual suffering from Gitelman's syndrome.

25
26 18. The method of claim 17, wherein the individual carries a mutation in at least one copy of
27 a gene encoding a thiazide sensitive Na-Cl cotransporter.

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29 19. The method of claim 18, wherein the gene is the *NCC* gene.

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31 20. The method of claim 19, wherein the mutation is a G738R mutation.

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21. The method of claim 18, wherein the individual carries a mutation in one copy of the gene.
22. The method of claim 18, wherein the individual carries a mutation in both copies of the gene.
23. A method of treating cystinuria or alleviating the symptoms of cystinuria, comprising administering an agent that permits the release of proteins from the endoplasmic reticulum.
24. The method of claim 23, further comprising the step of:
providing an individual suffering from cystinuria.
25. The method of claim 24, wherein the providing step comprises providing an individual suffering from type I cystinuria.
26. The method of claim 24, wherein the individual carries a mutation in at least one copy of a gene encoding a subunit of an rBAT protein.
27. The method of claim 26, wherein the individual carries a mutation in one copy of the gene.
28. The method of claim 26, wherein the individual carries a mutation in both copies of the gene.
29. The method of any of claims 3, 12, 17, or 24, wherein the agent is a calcium pump inhibitor.
30. The method of any of claims 3, 12, 17, or 24, wherein the agent decreases or inhibits the activity of UDP glucose:glycoprotein glycosyl transferase.

- 1 31. The method of any of claims 3, 12, 17, or 24, wherein the agent decreases or inhibits
2 activity of the endoplasmic reticulum Ca^{++} ATPase.
3
- 4 32. The method of any of claims 3, 12, 17, or 24, wherein the agent lowers the concentration
5 of Ca^{++} in the endoplasmic reticulum.
6
- 7 33. The method of any of claims 3, 12, 17, or 24, wherein the agent causes release of Ca^{++}
8 from the endoplasmic reticulum.
9
- 10 34. The method of any of claims 3, 12, 17, or 24, wherein the agent stimulates or increases
11 IP_3 receptor activity.
12
- 13 35. The method of any of claims 3, 12, 17, or 24, wherein the agent decreases or inhibits
14 calnexin functional activity
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- 16 36. The method of any of claims 3, 12, 17, or 24, wherein the agent increases or activates
17 ryanodine receptor activity
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- 19 37. The method of any of claims 3, 12, 17, or 24, wherein the agent comprises thapsigargin or
20 a derivative thereof.
21
- 22 38. The method of any of claims 3, 12, 17, or 24, wherein the agent comprises DBHQ or a
23 derivative thereof.
24
- 25 39. The method of any of claims 3, 12, 17, or 24, wherein the agent comprises cyclopiazonic
26 acid or a derivative thereof or wherein the agent comprises halothane or a derivative thereof.
27
- 28 40. The method of any of claims 3, 12, 17, or 24, wherein the agent permits release of
29 mis-assembled or mis-folded proteins from the endoplasmic reticulum.
30

- 1 41. The method of any of claims 3, 12, 17, or 24, wherein the agent is an oligonucleotide
2 which is antisense to a protein selected from the group consisting of UDP
3 glucose:glycoprotein glycosyl transferase, calnexin and Ca^{++} ATPase.
4
- 5 42. A method of treating any disease or clinical condition, comprising
6 administering an agent that permits the release of proteins from the endoplasmic
7 reticulum, wherein the agent increases or activates ryanodine receptor activity.
8
- 9 43. The method of claim 42, wherein the disease is selected from the list consisting of:
10 Cystic Fibrosis, Chronic Obstructive Pulmonary Disease, Paroxysmal Nocturnal
11 Hemoglobinuria, Familial Hypercholesterolemia, Tay-Sachs Disease, viral diseases,
12 neoplastic diseases, Hereditary Myeloperoxidase Deficiency, Congenital Insulin Resistance,
13 Rhinosinusitis, Nephrogenic Diabetes Insipidus, Hemochromatosis, Gitelman's Syndrome,
14 and Cystinuria.
15
- 16 44. A method of releasing a mis-assembled or mis-folded glycoprotein from the endoplasmic
17 reticulum of a cell comprising the step of administering an agent that decreases or inhibits the
18 functional activity of UDP glucose:glycoprotein glycosyl transferase.
19
- 20 45. A method of releasing a mis-assembled or mis-folded glycoprotein from the endoplasmic
21 reticulum of a cell comprising the step of administering an agent that decreases or inhibits
22 activity of the endoplasmic reticulum Ca^{++} ATPase.
23
- 24 46. A method of releasing a mis-assembled or mis-folded glycoprotein from the endoplasmic
25 reticulum of a cell comprising the step of administering an agent that lowers the concentration
26 of Ca^{++} in the endoplasmic reticulum.
27
- 28 47. A method of releasing a mis-assembled or mis-folded glycoprotein from the endoplasmic
29 reticulum of a cell comprising the step of administering an agent that decreases or inhibits
30 calnexin functional activity.
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- 1 48. A method of increasing the permeability of the apical surfaces of airway epithelial cells to
2 a chloride ion comprising the step of administering an agent that decreases or inhibits the
3 intracellular retention of mis-assembled or mis-folded glycoproteins.
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- 5 49. A method of increasing the permeability of the apical surfaces of airway epithelial cells to
6 a chloride ion comprising the step of administering an agent that decreases or inhibits the
7 activity of UDP glucose:glycoprotein glycosyl transferase.
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- 9 50. A method of increasing the permeability of the apical surfaces of airway epithelial cells to
10 a chloride ion comprising the step of administering an agent that decreases or inhibits activity
11 of the endoplasmic reticulum Ca^{++} ATPase.
12
- 13 51. A method of increasing the permeability of the apical surfaces of airway epithelial cells to
14 a chloride ion comprising the step of administering an agent that lowers the concentration of
15 Ca^{++} in the endoplasmic reticulum.
16
- 17 52. A method of increasing the permeability of the apical surfaces of airway epithelial cells to
18 a chloride ion comprising the step of administering an agent that decreases or inhibits
19 calnexin functional activity.
20
- 21 53. A method of screening candidate compounds to identify an agent that inhibits
22 endoplasmic reticulum-associated retention or degradation of a mis-assembled or mis-folded
23 glycoprotein, wherein the method comprises the steps of:
24 a). treating a cell exhibiting intracellular retention of a mis-assembled or mis-
25 folded glycoprotein in the endoplasmic reticulum with the candidate compound; and
26 b). determining whether the mis-assembled or mis-folded glycoprotein is released
27 from the endoplasmic reticulum, thereby identifying the candidate compound as an agent that
28 causes the release of a malformed mis-folded glycoprotein from the endoplasmic reticulum.
29

1 54. A method of screening candidate compounds to identify an agent that inhibits the
2 functional activity of UDP glucose:glycoprotein glycosyl transferase, wherein the method
3 comprises the steps of:
4 a). treating a cell exhibiting intracellular retention of a mis-assembled or mis-
5 folded glycoprotein in the endoplasmic reticulum with the candidate compound; and
6 b). determining whether the mis-assembled or mis-folded glycoprotein is released
7 from the endoplasmic reticulum, thereby identifying the candidate compound as an agent that
8 causes the release of a mis-assembled or mis-folded glycoprotein from the endoplasmic
9 reticulum.
10
11 55. A composition which comprises two or more agents selected from the group consisting of
12 an agent that decreases or inhibits the activity of UDP glucose:glycoprotein glycosyl
13 transferase, an agent that decreases or inhibits activity of the endoplasmic reticulum Ca^{++}
14 ATPase, an agent that stimulates or increases IP_3 receptor activity, and an agent that decreases
15 or inhibits calnexin functional activity.
16
17 56. A composition comprising an aerosol formulation of thapsigargin, DBHQ or
18 cyclopiazonic acid.